**Remarks/Arguments:**

Applicants wish to thank Primary Examiner Patricia A. Duffy for reconsidering the finality of the Office Action mailed June 21, 2005 (as requested by applicants), and consequently withdrawing the finality, as indicated in the instant Office Action. Additionally, applicants wish to thank the examiner for the courteous consideration rendered their undersigned representative in connection with the interview (by telephone) on 1 February 2006, during which the examiner had indicated that applicants' request to withdraw finality of the Office Action would be granted, as recorded in the Interview Summary mailed February 7, 2006. Lastly, applicants wish to thank the examiner for expressly setting forth withdrawn rejections in the instant Office Action.

Claims 20, 21, 24, 25, and 27-30 are pending.

Claims 1-19, 22, 23, 26, and 31-60 are cancelled, without prejudice or disclaimer.

Claim 20 is hereby amended by incorporating the subject matter of claim 23 and as described in the present specification (paragraph bridging pages 7 and 8). Additionally, claim 20 is amended by deleting (at line 3) the word "mutation" and, otherwise, to more clearly define the invention.

Claim 21 is hereby amended to incorporate subject matter of present claim 22 and as described in the present specification (paragraph bridging pages 7 and 8). Other changes were made, hereby, to claim 21 in order to more clearly define the invention.

Claims 20, 21, 24, and 25 are hereby amended to more clearly define the invention in view of the rejection of these claims under §112, ¶2. Taken together, the changes to the rejected

claims—effected hereby—resolve all issues raised in the rejection under §112, ¶2, as further explained below.

Claims 20 and 21 remain rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement. Reconsideration is requested in view of the changes to the rejected claims effected hereby.

Presently amended claims 20 and 21 incorporate the subject matter of claims 23 and 22, respectively, as indicated above. Since neither claim 22 nor claim 23 is included in the instant rejection, the rejection is overcome. Withdrawal of the rejection under §112, ¶1, for allegedly failing to comply with the written description requirement appears to be in order for withdrawal.

Claims 27-30 were rejected under 35 USC 112, first paragraph, as allegedly lacking enablement. Reconsideration is requested, in view of the Rule 132 declaration, submitted concurrently herewith.

According to the statement of rejection, the rejection can be overcome by submitting a declaration (by the Assignee of record) that provides—with respect to the deposit of clones pDF3 and pDF4 described at page 5 of the present specification—sufficient assurance that all required deposits have been made and all the conditions of 37 CFR 1.801-809 have been met; which, if the deposit was made under the Budapest Treaty, is satisfied by filing a declaration by the assignee of record that the deposit was accepted by an International depository authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposit will be irrevocably

removed upon the grant of a patent on the subject application and that the deposit will be replaced if viable samples cannot be dispensed by the depository.

As required by the statement of rejection, submitted herewith is the requisite declaration by the assignee of record (under PTO Rule 108). Also submitted herewith are copies of the deposit receipts—with corresponding English translations (verified). Withdrawal of the rejection for alleged lack of enablement appears to be in order.

Claims 20-25 were rejected under 35 USC 112, ¶2, for allegedly being indefinite. Reconsideration is requested, in view of the instant amendments to the rejected claims and the following remarks.

Claims 20 and 25 are rewritten to clarify that the "nucleic acid sequence" recited in claim 20 is—in claim 25—selected from among the SEQ ID NOS in the Markush group recited in claim 25. In a similar manner, claims 21 and 24 are rewritten hereby.

Under §112, ¶2, claim 24 is specifically rejected for reciting "SEQ ID NO: 10" and "SEQ ID NO: 11" as alternative species of the "nucleic acid sequence"—recited in claim 21. Applicants submit that SEQ ID NOS: 10 and 11 correspond to nucleotides 426 to 401 and 427 to 402, respectively, of SEQ ID NO: 1 (specification, page 13); and, as such, SEQ ID NO: 10 hybridizes to the sequence complementary to nucleotides 426 to 401 of SEQ ID NO: 1, and SEQ ID NO: 11 hybridizes to the sequence complementary to nucleotides 427 to 402 of SEQ ID NO: 1. Accordingly, SEQ ID NOS: 10 and 11 constitute species of the "nucleic acid sequence" *subgenus* "a sequence derived from SEQ ID NO: 1." In other words, each of SEQ ID NO: 10 and SEQ ID NO: 11 is a

species of both the "nucleic acid sequence" (genus) and the "sequence derived from SEQ ID NO: 1 (subgenus) and, so, claim 24 satisfies the requirements of §112, ¶2.

For the foregoing reasons applicants submit that the rejection of claims 20-25 under §112, 2nd ¶, is overcome. Withdrawal of the rejection appears to be in order.

Claims 20 and 25 were rejected under 35 USC 102(b) as being allegedly anticipated by *DNA Research, 5*, 1-9 (1998) (Makino). Reconsideration is requested.

First of all, applicants incorporate herein by reference their arguments traversing the rejection set forth in the amendment filed November 17, 2005. Particular attention is directed to the fact—unchallenged by the PTO—that the public did not have possession of plasmid "pO157"—the allegedly anticipating material disclosed in Makino—until April 27, 1999, i.e., the publication date of AB 011549/C, the only evidence provided by the examiner to show that the plasmid pO157 meets the nucleotide sequence" recited in the rejected claims. The public did not have possession of the plasmid pO157 until the plasmid was sequenced, correctly, and this correct sequence was published (or otherwise known) in accordance with §102(b). For example (hypothetically), if a journal article identified "widget X" as being available on request and states that a description of widget X "will appear in the ACME widget databases," but widget X was described, incorrectly, in the ACME widget databases, the public did not have possession of widget X by virtue of the journal article, since the journal article provided—by reference—an incorrect description of the widget. Since the journal article incorrectly describe widget X, the only way a member of the public could possess widget X would be to obtain the widget, itself.

Secondly, alleging that applicants' argument is "clearly erroneous" because it "misstated the rejection as in view of and not 'in light of,'" reduces applicants' argument to a matter of semantics and, so, completely misses the point of applicants' argument. The argument points out that Makino, by itself, is not "a printed publication" in which "the ["nucleic acid"] invention was . . . described," under §102(b) and, therefore, claims 20 and 25 cannot be rejected for lack of novelty—under §102(b)—based on Makino.

Notwithstanding the impropriety of the rejection under §102(b) based on Makino, the rejection is overcome by the foregoing amendments to the rejected claims, in any event. Claim 20 is amended by deleting—as one of the alternatives defining the claimed "isolated nucleic acid"—the sequence derived from SEQ ID NO: 2 "by mutation." Since this "mutation" alternative is that allegedly met in Makino, the rejection under §102(b) based on Makino is rendered moot. Withdrawal of the rejection appears to be in order.

Claim 20 was rejected under 35 USC 102(b) as being allegedly anticipated by Brunder. Reconsideration is requested.

According to the statement of rejection "deletion of single 'mutation' from the claim would obviate the 102 issue with respect to Brunder." The "mutation" alternative has been deleted from claim 20, as explained above. Therefore, according to the statement of rejection, the rejection of claim 20 under §102(b) is overcome and, therefore, withdrawal of the rejection appears to be in order.

Claims 20-25 were rejected under 35 USC 103(a) as being allegedly unpatentable over Makino in view of Schmidt and Kennell "in light of" GenEMBL Accession Number AB 011549. Reconsideration is requested.

The statement of rejection alleges "there is nothing unobvious about using fragments of an existing plasmid to detect the plasmid *per se* or the organism from which it was derived." The allegation is incorrect because it assumes that any fragment derived from the plasmid pO157 may be used to specifically detect organisms containing the plasmid, which assumption is incorrect as shown, e.g., by Brunder (relied on to reject claim 20 under §102(b)).

Brunder teaches that the *katP* gene, which was identified on plasmid pO157 of a EHEC O157:H7 strain, is also found in 2 out of 12 non-O157 shiga-like-toxin-producing *E. coli* (SLTEC) (see Brunder table 2, page 3312). Therefore, the *katP* gene, which is found on plasmid pO157, does not enable specific detection of an organism containing the plasmid.

On the other hand, the invention of present claim 21 provides SEQ ID NO: 1, which results from the stable combination of a portion of IS91 with *katP*. The results provided in the instant application show that SEQ ID NO: 1 is a specific marker of pO157-containing EHECs. In particular, the specificity study described in the present specification (from page 22, line 11, to page 24, line 10) demonstrates that the stable combination of IS91 with *katP* is (1) detected in all of the 56 pO157-containing EHEC strains tested (O157:H7 and O157:H-) and (2) absent from any of the other assayed strains of, i.a., enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC) *E. coli*, Salmonelia, and Shigelia.

The detection of the combination of a portion of IS91 with *katP,* thus, enables specific detection of EHECs containing the pO157 plasmid.

Furthermore, applicants submit that the skilled person would not have selected a sequence including an insertion sequence (IS) for further evaluation as a putative stable marker of pO157-containing EHECs. Indeed, as stated by Makino (page 6, 1st complete 1¶), "Insertion sequences (ISs) are a large group of bacterial transposable DNA elements. These cause various kinds of genome rearrangements, such as deletions, inversions, duplications and replicon fusions, by their ability to transpose."

Accordingly, the skilled person would have expected further genome rearrangements to occur in time, in a region containing an insertion sequence. Hence, the skilled person would not have selected such a possibly unstable region as a marker.

However, the present inventors demonstrated that the combination of a portion of IS91 with *katP* is stable, i.e., by a specificity study in which the IS91/*katP* combination was found to be conserved in EHECs O157:H7 of various origins (specification page 5, lines 33-36, and page 22, line 11 - page 24, line 10). This stability is believed to be associated with the lack of inverted repeats in the IS91 portion, which repeats are required for transposition of the insertion sequence (present specification, page 5, lines 28-32).

The "nothing unobvious" allegation is also incorrect because it does not take into account that the sequence SEQ ID NO: 2 was identified on the plasmid pO157, but that it, nevertheless, enables detection of a particular group of EHECs, including EHECs that do not contain the plasmid pO157.

Indeed, the specificity study described in the subject application (pages 25-26) shows that the primer pair SEQ ID NO: 21/SEQ ID NO: 22, which enable specific amplification of SEQ ID NO: 2, achieve detection of any enterohaemorrhagic *E. coli* strain possessing the genotype $vt^+$ (verotoxin), $eae^+$ (Intimin), or $ehly^+$ (enterohaemolysin).

Therefore, detection of SEQ ID NO: 2 makes it possible to specifically detect, with a single amplification reaction, this group of EHECs (above); whereas, detection of $vt^+$, $eae^+$, and $ehly^+$ EHECs previously required the use of several molecular systems (present specification, page 6, lines 18-29).

It would not have been obvious—under §103(a)— for the skilled person to identify that the plasmid pO157 would contain a sequence allowing detection of any EHEC O157:H7 and, more broadly, any EHEC $vt^+$, $eae^+$, and $ehly^+$. Accordingly, withdrawal of the rejection under 35 USC 103(a) appears to be in order.

Favorable action is requested.

Respectfully submitted,

JACOBSON HOLMAN PLLC

By _____

William E. Player
Reg. No. 31,409

400 Seventh Street, NW
The Jenifer Building
Washington, D.C. 20004
Tel. (202) 638-6666
Fax (202) 393-5350
Date: August 29, 2007
WEP/jhr
R:\Home\WPLAYE\wep&secretary\2007\November\P66034US0 amd(rce).wpd